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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/085,853	10/18/2001	Bertrand Merot	14138.1USD1	3281

23552 7590 05/07/2003

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EXAMINER

MAYES, LAURIE A

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/085,853

Applicant(s)

MEROT ET AL.

Examiner

Laurie Mayes

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 43-52 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 43-52 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☒ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☒ Certified copies of the priority documents have been received in Application No. 08/983,564.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 43-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The language “or variants thereof” is indefinite and could comprise a protein with 0-4+ globin chains. The language “having the capacity to reversibly bind oxygen” is indefinite as it is unclear if there are upper and lower limits of reversible binding ability implied by such terminology.

The meaning of “tile pyrole rings” in claim 44 is unclear.

In claim 46, it is unclear whether the N-terminal signal peptide is in combination with a vacuolar targeting signal or whether the N-terminal signal peptide is a separate entity from the N-terminal signal peptide.

### ***Claim Objections***

Claim 47 is objected to as the terms “methionine” and “terminal” are misspelled. Claim 48 is objected to as the term “polypeptide” is misspelled.

### ***Objections to Specification***

The specification is objected to as it recites canceled claims (p. 17, 3<sup>rd</sup> paragraph). Also, sequences appear in the specification without the required corresponding SEQ ID NO:, for example, see. p. 23, lines 13-15.

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The use of trademarks, for example, SEQUENASE (p. 24, line 11 and p. 28, line 4), GENE CLEAN (p. 25, line 6, p. 26, last line and p. 27, bottom of page and on p. 28-30, 33, 34, 37, 38, etc.), CROCODILE II (p. 26, bottom of page), has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

#### *Oath/Declaration*

The declaration is objected to as it was not executed in accordance with either 37 CFR 1.66 or 1.68 as it was signed by one inventor only (Gruber).

#### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 43-46 and 48, 49, 51 and 52 are rejected under 35 U.S.C. 102(a) as being anticipated by Dieryck et al. (Transfusion Clinique et Biologique, V. 2, N. 6, 1995, pp. 441-447; see English translation). Please note that the reference's authors are not the same as the inventive entity of the present application. Dieryck et al. teach the expression of recombinant

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human hemoglobin in plants (summary, p. 2 of translation). Dieryck et al. teach the advantages of low production costs and innocuousness of making human hemoglobin in plants (p. 2, lines 4-12) wherein the transgenic protein contains a nucleus of plant origin (p. 7, first para.) and at least one polypeptide chain of animal origin (p. 2, last two lines)(present claim 43). Hemoglobin is known to have alpha and beta globin chains and a heme molecule, protoporphyrin IX, for example, which reversibly binds oxygen. (US 6,344,600; this reference is cited only to demonstrate what inherent properties of hemoglobin that are widely known in the art.)(claims 44, 45, 47, 48, 49). Dieryck et al. also teach the above-described protein comprising a vacuolar targeting signal (p. 6, 2<sup>nd</sup> para.)(present claim 46) and using the protein in blood transfusions wherein blood is a biologically acceptable carrier for the protein (p. 2, line 1)(present claims 51 and 52). It is known in the art that transfusions may be used to treat conditions requiring an improvement in the transport of oxygen in the blood. (US 5,498,421; col. 3, lines 25-31). Thus, all of the elements of claims 43-46 and 48, 49, 51 and 52 are taught by Dieryck et al. and these claims are anticipated under 35 U.S.C. 102(a).

It is also noted that mature eukaryote proteins usually lack an NH2 terminal methionine.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 43, 45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dieryck et al. (Transfusion Clinique et Biologique, V. 2, N. 6, 1995, pp. 441-447 ; see English translation). Dieryck et al. teach the expression of recombinant human hemoglobin in plants (summary, p. 2 of translation). Dieryck et al. teach the advantages of low production costs and innocuousness of making human hemoglobin in plants (p. 2, lines 4-12) wherein the transgenic protein contains a nucleus of plant origin (p. 7, first para.) and at least one polypeptide chain of animal origin (p. 2, last two lines). Dieryck et al. do not teach specifically a protein wherein a globin chain lacks an NH<sub>2</sub>-terminal methionine. However, Dieryck et al. do teach the N-terminal methionine modifies the response to allosteric factors and the methionine disturbs the binding site of organic phosphates and that human hemoglobin has been transgenically produced without the N-terminal methionines (p. 3, 1<sup>st</sup> para.). Thus, it would have been obvious to one of ordinary skill in the art at the time of the invention to remove the NH<sub>2</sub> terminal methionine to encourage binding to improve the transport of oxygen in the blood. Thus, the claimed invention was prima facie obvious to make and use at the time the claimed invention was made.

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Claims 43 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dieryck et al. in view of Garlick et al. (US 5,521,154). Dieryck et al. teach the expression of recombinant human hemoglobin in plants (summary, p. 2 of translation). Dieryck et al. teach the advantages of low production costs and innocuousness of making human hemoglobin in plants (p. 2, lines 4-12) wherein the transgenic protein contains a nucleus of plant origin (p. 7, first para.) and at least one polypeptide chain of animal origin (p. 2, last two lines). Dieryck et al. do not teach a protein that binds oxygen with an affinity of between 7 and 40 mm Hg.

Garlick et al. teach that hemoglobin with an oxygen affinity of at least 13 mm Hg (col. 3, lines 33-35) may be used as an oxygen-carrier (col. 3, lines 40-41). Given the success of carrying oxygen for hemoglobin with an oxygen affinity of at least 13 mm Hg, it would have been obvious to one of ordinary skill in the art at the time of the invention to make transgenic hemoglobin as taught by Dieryck that also has an oxygen binding affinity of at least 13 mm Hg for use as an oxygen carrier. Thus, the claimed invention was prima facie obvious to make and use at the time the claimed invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laurie Mayes whose telephone number is (703) 605-1208. The examiner can normally be reached on Monday through Friday from 9 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1123.



Laurie Mayes  
Patent Examiner  
Art Unit 1653  
May 2, 2003



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